and mortality. In our institution, 734 patients received an UCBT between 2000 and 2010. The focus of this study was 76 patients (10.4%) who had primary (n = 55) or secondary (n = 21) GF. Primary GF was defined as failure to achieve an absolute neutrophil count (ANC) ≥ 500/mcL for 3 consecutive by day +42 or chimerism <5% in all assessments after transplantation regardless of ANC. Secondary GF was defined as loss of chimerism <5% after having achieved 5% or more after UCBT, or ANC persistently below 500/mcL after having achieved ≥ 500/mcL for 3 consecutive days by day +42. Patients were grouped as those with malignant disease/myeloablative conditioning (MA, n = 28), malignant disease/nonmyeloablative conditioning (NMA, n = 26) and non-malignant disease (non-Malig, n = 22). The OS at 100 days for patients with primary GF was 49%(95%CI, 35-61%) and secondary GF was 76%(95%CI, 52-89%) (p = 0.03). Thirty-nine patients underwent a second transplant at a median time of 50 days (range: 32-565). Excluding patients with slow primary engraftment (n = 10), who were counted as primary GF, the remaining 27 patients were considered too ill to withstand a second transplant. Second transplant conditioning included: no additional conditioning (n = 10), ATG/ALG ± steroids (n = 11), and chemotherapy ± ATG/ALG (n = 18). Cumulative incidence of engraftment after 2nd transplant was 77% at a median time of 16 days (range: 0-39). Engraftment was similar in all groups. After 2nd transplant, OS was 69%(95%CI, 52-81%) at 100 days and 41%(95%CI, 26-56%) at 1 year. The day 100 survival was 32%(95%CI, 16-49%) for MA, 73%(95%CI, 52-86%) for NMA and 68%(95%CI, 45-83%) for non-Malig patients(p = 0.01). In evaluation of time to second transplant, the OS at 100 days was similar for patients transplanted ≤ 50 or > 50 days: (62%[95%CI, 38-79%] vs. 78% [95%CI, 51-91%] respectively, p = 0.31); there was also no difference in OS at 1 year (33%[95%CI, 15-53%] vs. 50%[95%CI, 26-70%] respectively, p = 0.34). The most frequent causes of death at day 100 after 2nd transplant were: second graft failure, bacterial infection and disease recurrence. In conclusion, patients with primary or secondary GF after UCBT who undergo a second transplant have encouraging survival with over 40% surviving 1 year, and identifying strategies to overcome graft failure will help to improve upon this.

350

EXPRESSION OF α4β7 INTEGRIN ON PERIPHERAL BLOOD MEMORY CD4+ T-CELLS AFTER ALLOGENEIC HCT CORRELATES WITH NON-RELAPSE MORTALITY AND OVERALL SURVIVAL

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Background: Surface expression of α4β7 integrin, a gut-homing lymphocyte trafficking molecule, on peripheral blood memory T-cells has been shown to be increased in patients who develop acute intestinal graft-vs.-host disease (GVHD) after allogeneic hematopoietic cell transplantation (HCT). Decreased expression of α4β7 integrin on regulatory T-cells at engraftment has also been shown to correlate with the development of intestinal GVHD. We hypothesized that α4β7 integrin expressing memory T-cells in the peripheral blood at day +15 and day +30 after HCT would be associated with the development of acute intestinal GVHD and survival outcomes.
Methods: Serial samples at day +15 and day +30 from 84 patients undergoing either RIC or myeloablative conditioning allogeneic HCT with peripheral blood stem cells were analyzed. Median follow-up was 661 days (range 39, 907 days) among survivors. T-cell subsets chosen for analysis included naïve and memory (defined by expression of CD45RA and CD45RO, respectively) CD4+ and CD8+ T-cells. Expression of α4β7 integrin was assessed by flow cytometry.
Results: Increased percentage of memory CD4+ T-cells expressing α4β7 integrin at day +15 correlated with increased non-relapse mortality (NRM) (p = 0.005) and decreased overall survival (OS) (p = 0.016). The cumulative incidence of NRM was 25% (21 / 84) (95% CI 16%, 34%) in this cohort. Expression on any naïve T-cell subset, on memory CD8+ T-cells, or at day +30 was not shown to correlate with outcomes. Further analysis showed that conditioning intensity, donor type, GVHD prophylaxis regimen, use of in vivo T-cell depletion, and underlying disease had no significant effect on the % of memory CD4+ T-cells expressing α4β7 integrin. Expression of α4β7 integrin on any T-cell subset did not correlate with the development of acute intestinal GVHD, although there were only 5 cases of grade II and 7 cases of grades III-IV disease in this cohort.
Conclusion: Expression of α4β7 integrin on memory CD4+ T-cells at day +15 after HCT predicts for NRM and OS. Analysis with a larger number of samples is planned to confirm these results, but continued study of α4β7 integrin as a biomarker or target of intervention after HCT is warranted. This biomarker may be valuable in identifying a high risk subset of patients who could benefit from pre-emptive organ specific targeted intervention.

351

OUTCOME OF ALLOGENEIC STEM CELL TRANSPLANT IN MYELODYSPLASTIC SYNDROMES WITH MONOSOMAL KARYOTYPE: AN ADVERSE PROGNOSTIC FACTOR IN ADDITION TO CONVENTIONAL UNFAVORABLE KARYOTYPE

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Introduction: Monosomal karyotype (MK) is defined as the presence of two or more distinct autosomal monosomies or a single monosomy associated with a structural abnormality. It was first described as an adverse prognosis for acute myeloblastic leukemia. Recently, Patnaik et al demonstrated adverse prognostic effect of MK in myelodysplastic syndromes (MDS). However, the effect of MK on the allotransplant in MDS is not yet well described.
Methods: MDS patients who underwent allotransplant at the University of Iowa from 1990 to 2009 were retrospectively reviewed. Cytogenetic and patient's data were abstracted from medical genetics and transplant database. Patients were classified according to

Table 1. Demographic data of MDS patients underwent allogeneic HCT

	N = 79
Median Age at diagnosis, years (Range)	49.7 (19-65)
Median Age at transplant, years (Range)	51.0 (20-66)
Gender, M/F	43/36
IPSS[#]	
High	17 (21.5%)
High Intermediate	40 (50.6%)
Low Intermediate	18 (22.8%)
Low	4 (5.1%)
Disease status at transplant	
Complete remission	10 (12.7%)
Residual or active hematologic disease	69 (87.3%)
HCT-CI	
0	22 (27.8%)
1-2	15 (20.0%)
≥3	42 (52.2%)
HLA compatability	
6/6 or 8/8	65 (72.3%)
4/6, 5/6 or 7/8	14 (27.7%)
Donor	
Related	39 (49.4%)
Unrelated	40 (5.6%)
IPSS Cytogenetic classification	
Favorable	26 (32.9%)
Intermediate	16 (20.2%)
Unfavorable*	37 (46.8%)
Monosomal karyotype	24 (30.4%)

[#]Internation Prognostic Scoring System.
*Unfavorable karyotypes include complex cytogenetic abnormality (≥3 structural abnormalities) or abnormal chromosome 7.

cytogenetic abnormalities (favorable, intermediate or unfavorable risk group) based on International Prognostic Scoring System (IPSS). We evaluated allotransplant outcome in MDS patients with MK.

Result: A total of 79 MDS patients who underwent allotransplant were identified. Thirty seven of 79 patients (46.8%) harbored unfavorable karyotypes (23 complex karyotype, 25 abnormal chromosome 7). Of 79 patients, 24 (30%) met the criteria of MK. The median follow-up was 5.1 months (0-242 mo). Twenty-four patients (30%) relapsed and 59 (74.7%) died during the follow-up duration. Major causes of death included infection (24%), graft versus host disease (25%) and relapse (31%). Two-year relapse incidence (RI) and overall survival (OS) were 36% (95%CI, 23%-49%) and 32% (95% CI, 22%-43%) respectively. Of 79 patients, patients with MK had significantly higher 2-year RI (51% VS 28%; $p = 0.01$) (95%CI, 28-75% VS 13-43%) and lower 2-year OS (6% VS 41%; $p = 0.02$) (95%CI, 0-24% VS 28-54%) than patients without MK. Due to significant overlap between MK and unfavorable karyotypes, we further analyzed the effect of MK in each unfavorable karyotype composite (unfavorable with MK VS unfavorable without MK). Although the outcome was not statistically different, patients with both unfavorable karyotype and MK had a trend toward higher 2-year RI (51% VS 38%, hazaard ratio [HR] 1.7, $p = 0.34$) and lower 2-year OS (6% VS 31%, HR 1.5, $p = 0.28$) compare with patients with unfavorable karyotypes without MK.

Conclusion: MK is associated with poor allotransplant outcome with high relapse incidence and low overall survival in addition to IPSS unfavorable cytogenetic abnormalities.

352

MELPHALAN 140MG/M^2 COMBINED WITH TBI2(4)Gy AND FLUDARABINE 125MG/M^2 AS CONDITIONING FOR ELDERLY PATIENTS WITH HEMATOLOGICAL MALIGNANCIES IN UNRELATED BONE MARROW TRANSPLANTATION IS COMPARABLE IN SAFETY AND EFFECTIVENESS WITH TBI/CY FOR YOUNGER PATIENTS

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Background: The optimal conditioning and dosage regimen for unrelated bone marrow transplantation for elderly patients with hematological malignancies remains unknown.

Objective and Methods: Among the 63 cases of unrelated bone marrow transplantation for hematological malignancies performed in our department, we compared and examined the safety and efficacy of the most commonly used conditioning regimen for elderly patients, i.e., fludarabine (Flu) (125mg/m^2) + melphalan (Mel) (140mg/m^2) + total body irradiation (TBI) [2(4)Gy] (22 cases; hereafter Flu/Mel/TBI group), with the TBI (12Gy) + cyclophosphamide (CY) (120mg/kg) regimen (23 cases; hereafter TBI/CY group). For 3 cases in the Flu/Mel/TBI group, TBI was increased to 4Gy from 2Gy due to myelodysplastic syndrome associated with each of myelofibrosis, splenomegaly, and aplastic anemia.

Results: The mean age of patients was 58.5 years (range, 40-66 years) for the Flu/Mel/TBI group and 40 years (range, 21-57 years) for the TBI/Cy group, with the Flu/Mel/TBI group being significantly older ($p = 0.002$). Acute lymphoblastic leukemia was common in the TBI/CY group. The number of high risk cases did not significantly differ between the two groups (Flu/Mel/TBI group, 50%; TBI/CY group, 30%). There were no differences in the number of days required for engraftment or to achieve complete donor chimerism. Early adverse events higher than grade 3, and bacterial, fungal, or viral infections within one year were 72.7%, 45.5%, 18.2%, and 45.5% in the Flu/Mel/TBI group, and 73.9%, 26.1%, 17.4%, and 52.2% in the TBI/CY group, with no significant difference between the groups. Acute and chronic GVHD were observed in 56.5% and 81% of cases in the Flu/Mel/TBI group, and 52.5% and 53.4% in the TBI/CY group, with the Flu/Mel/TBI group having a significantly higher incidence of chronic GVHD ($p = 0.014$). The median observation period of survivors was 30 months for the Flu/Mel/TBI group and 68 months for the TBI/CY group. Two year overall survival and relapse-free survival were 72.4% and 59.1% in the Flu/Mel/TBI group, and 77.5% and 64.1% in the TBI/CY group; and two year treatment-related mortality and recurrence rate were 14.6% and 30.8% in the Flu/Mel/TBI group, and 0% and 35.9% in the TBI/CY group, with no significant differences between the groups.

Conclusion: Flu/Mel/TBI for elderly individuals with hematological malignancies proved to be as effective and safe as TBI/CY for younger patients.

353

A PROSPECTIVE RANDOMIZED STUDY COMPARING REDUCED-INTENSITY CONDITIONING AND MYELOABLATIVE CONDITIONING IN PATIENTS WITH MYELOID LEUKEMIA UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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There have been no randomized studies comparing myeloablative conditioning (MAC) and reduced-intensity conditioning (RIC) in allogeneic hematopoietic stem cell transplantation (HSCT). We wanted to compare the safety and efficacy of these two regimens.

We performed an open-labeled, randomized, controlled phase-III trial. Over a 10-year period, adult patients ≤60 years of age with myeloid leukemia were randomised (1:1) to undergo RIC (n = 18) or MAC (n = 19). We included recipients of HLA-A, HLA-B, or HLA-DRB1-identical unmanipulated grafts from related or unrelated donors. The primary endpoint was transplant-related mortality (TRM). Secondary endpoints included relapse, survival, chimerism, and toxicity.

The RIC patients had faster platelet engraftment ($p<0.01$), required fewer erythrocyte and platelet transfusions ($p<0.001$), and required less total parenteral nutrition (TPN) than the MAC group ($p<0.01$). Cytomegalovirus reactivation was commoner in the MAC group (14/19) than in the RIC group (6/18) ($p = 0.02$). Hemorrhagic cystitis occurred in eight of the MAC patients and in none of the RIC patients ($p<0.01$). Donor chimerism was similar in the two groups regarding CD19 and CD33, but was delayed for CD3 in the RIC group. Later chimerism status was similar. Incidences of acute and chronic graft-versus-host disease (GVHD) were similar in the two groups, but two MAC patients and no RIC patients died of GVHD. Five-year TRM was around 11% in both groups, and relapse and survival were not significantly different. The MAC patients with intermediate cytogenetic acute myeloid leukemia had a three-year survival of 73%, as compared to 90% in the RIC patients.

TRM was low with RIC and MAC. Although few patients were included, RIC had several advantages such as faster platelet engraftment, fewer transfusions, less TPN, fewer CMV reactivations, and less hemorrhagic cystitis.

354

OUTCOME OF HIGH-RISK AND REFRACTORY AML/MDS PATIENTS RECEIVING A FLAMSA SEQUENTIAL CHEMOTHERAPY REGIMEN FOLLOWED BY REDUCED-INTENSITY CONDITIONING (RIC) AND ALLOGENEIC HEMATOPOEITIC STEM CELL TRANSPLANTATION (allo-HSCT)

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This retrospective analysis aimed to assess the outcome of 40 patients with refractory or high risk AML/MDS who received FLAMSA sequential chemotherapy. There were 30 males and 10 females with a median age of 52 years (32-66). Diseases characteristics were: progressive or refractory disease after rescue treatment for first relapse (n = 21), early relapse without any further salvage therapy (n = 4), and primary induction failure (n = 4). The series also included 7 patients with high risk MDS and 4 patients in first CR but having a very poor prognosis. The FLAMSA regimen included Fludarabine (30 mg/m^2/d), cytarabine (2 g/m^2/d) and amsacrine (100mg/m^2/d) from day -12 to day -9. After 3 days of rest, a RIC regimen was administered. In 28 patients, the RIC regimen included 4